Microbiological Associates
5221 River Road
Bethesda, Maryland 20016

Human Aryl Hydrocarbon Hydroxylase Studies.

The object of this study is to achieve a reproducible AHH assay system applicable to human subjects. The use of this assay may reveal a relationship between levels of AHH and carcinoma of the lung, as well as other cancers that have been assumed to be related to environmental carcinogens.

This past year, four methodologic changes have resulted in an assay for AHH activity in cultured human lymphocytes that is much more reproducible than any assay method previously available. These changes are: (1) use of human AB serum in the culture medium; (2) use of NADH-dependent cytochrome c reductase activity as the measure of total microsomal content in mitogen-activated lymphocytes; (3) correction for the percent of T lymphocyte cells in the initial assay culture; (4) use of frozen (-120° C) stored lymphocytes as source material of AHH determinations. This latter point is particularly important because it may offer a practicable method for analyzing the role of AHH activity in the cancer susceptibility in man. With proper confirmation in other laboratories these methodologic changes may permit an inquiry into genetic regulation of AHH levels and the role of these hydrocarbon metabolizing enzymes in cancer susceptibility in man.

In a related program, twin studies and family studies will be carried out in order to determine whether AHH levels are under some form of genetic control. In collaboration with Drs. H. Lynch and H. Guirgis (CU), lymphocyte samples from specific family members will be collected, stored at -120° C and assayed after accumulation of samples from families congenitally either susceptible or resistant to certain forms of cancer. The "Cancer Family Syndrome" population is characterized by an increased frequency of adenocarcinomas of all varieties, but predominantly adenocarcinomas of the endometrium and colon, increased frequency of multiple primary malignant neoplasms (20% greater), earlier age of onset of cancer as compared to its occurrence in the general population, and finally, autosomal dominant mode of inheritance. By analogy with in vivo model systems using inbred strains of mice, it is possible that in at least some of the cancer-prone families the rate-limiting factor controlling susceptibility may be their inherent capacity to metabolize chemical carcinogens.

Activation Date: January 1, 1978

Current Contract Level: $148,000.